PCT/EP00/08143
10/049976 #2

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4

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I also certify that by virtue of an assignment registered under the Patents Act 1977, the application is now proceeding in the name as substituted.

I also certify that the attached copy of the request for grant of a Patent (Form 1/77) bears an amendment, effected by this office, following a request by the applicant and agreed to by the Comptroller-General.

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Signed A M Brewer.

Dated 21 AUG 2000

GB9919500.0

By virtue of a direction given under Section 30 of the Patents Act 1977, the application is proceeding in the name of

AVENTIS CROPSCIENCE GMBH,
Brüningstrasse 50,
65929 Frankfurt am Main,
Federal Republic of Germany

[ADP No. 07950702001]

**Patents Form 1/77**

Patents Act (Rule 16)

THE PATENT OFFICE
18 AUG 1999
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1/77

19AUG99 E520453-2 D01777
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# Request for grant of a patent

*(See the notes on the back of this form. You can also get an explanatory leaflet from the Patent Office to help you fill in this form)*

**The Patent Office**

Cardiff Road
Newport
Gwent NP9 1RH

1. Your reference

99c112

2. Patent application number
*(The Patent Office will fill in this part)*

18 AUG 1999

**9919500.0**

3. Full name, address and postcode of the or of each applicant *(underline all surnames)*

Hoechst Schering AgrEvo GmbH
Miraustr. 54
D-13509 Berlin
Germany

SECTION 80 (1977 ACT) APPLICATION FILED 17/7/2000

Patents ADP number *(if you know it)*

If the applicant is a corporate body, give the country/state of its incorporation

Germany 66964620012

4. Title of the invention

FUNGICIDAL COMPOUNDS.

5. Name of your agent *(if you have one)*

"Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*

~~AgrEvo UK Limited~~
~~Patent Department~~
~~Chesterford Park~~
~~Saffron Walden~~
~~Essex CB10 1XL~~

Aventis CropScience UK dr
Patent Dept
Tyfield Road
Ongar
Essex CM5 0HW

51/77 dl 16-8-00

Patents ADP number *(if you know it)*

06512040003

6. If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or of each of these earlier applications and *(if you know it)* the or each application number

| Country | Priority application number *(if you know it)* | Date of filing *(day / month / year)* |
|---|---|---|

7. If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application

| Number of earlier application | Date of filing *(day / month / year)* |
|---|---|

8. Is a statement of inventorship and of right to grant of a patent required in support of this request? *(Answer 'Yes' if:*

*a) any applicant named in part 3 is not an inventor, or*
*b) there is an inventor who is not named as an applicant, or*
*c) any named applicant is a corporate body.*
*See note (d))*

Yes

**Patents Form 1/77**

9. Enter the number of sheets for the following items you are filing with this form. Do not count copies of the same document

| | |
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| Continuation sheets of this form | |
| Description | 21 |
| Claim(s) | 2 |
| Abstract | |
| Drawing(s) | |

10. If you are also filing any of the following, state how many against each item.

| | |
|---|---|
| Priority documents | |
| Translations of priority documents | |
| Statement of inventorship and right to grant of a patent *(Patents Form 7/77)* | |
| Request for preliminary examination and search *(Patents Form 9/77)* | |
| Request for substantive examination *(Patents Form 10/77)* | |
| Any other documents *(please specify)* | |

11. I/We request the grant of a patent on the basis of this application.

Signature [signature] Date 18-8-99

R.C. SEWELL

12. Name and daytime telephone number of person to contact in the United Kingdom 01799 573342.

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*b) Write your answers in capital letters using black ink or you may type them.*

*c) If there is not enough space for all the relevant details on any part of this form, please continue on a separate sheet of paper and write "see continuation sheet" in the relevant part(s). Any continuation sheet should be attached to this form.*

*d) If you have answered 'Yes' Patents Form 7/77 will need to be filed.*

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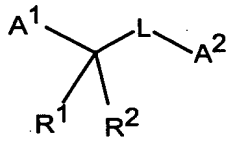
Fungicides

This invention relates to compounds having fungicidal activity.

In a first aspect the invention provides the use of a compound of general formula I and salts thereof as a phytopathogenic fungicide



(I)

wherein

$A^1$ is 2-pyridyl or its *N*-oxide, each of which may be substituted by up to four groups at least one of which is haloalkyl;

$A^2$ is heterocyclyl or carbocyclyl, each of which may be substituted, or acyl ($A^2$ is preferably optionally substituted phenyl, optionally substituted heterocyclyl or acyl);

L is a 4-atom linker selected from the list: $-N(R^5)C(=X)-X^1-CH(R^3)-$, $-N(R^5)C(=X)CH(R^3)CH(R^4)-$, $-N(R^5)C(=X)C(R^3)=C(R^4)-$, $-N(R^5)C(R^3)=C(R^4)-C(=X)-$, $-N(R^5)C(R^3)=C(R^4)-SO_2-$, $-N(R^5)C(=X)C(R^3)(R^4)-SO_2-$ and $-N(R^5)C(=X)C(R^3)(R^4)-X^1-$; wherein $A^1$ is attached to the left hand side of linker L;

$R^1$, $R^2$, $R^3$ and $R^4$, which may be the same or different, are $R^b$, cyano, nitro, halogen, $-OR^b$, $-SR^b$ or optionally substituted amino; or $R^1$ and $R^2$, or $R^3$ and $R^4$, together with the interconnecting atoms, may form a 3-, 4-, 5- or 6-membered ring, which may be substituted ($R^1$, $R^2$, $R^3$ and $R^4$ are preferably hydrogen, optionally substituted alkyl or acyl);

X is oxygen or sulfur;

$X^1$ is oxygen, sulfur or $-N(R^5)-$;

$R^5$ is $R^b$, cyano or nitro, or $R^5$ and $A^2$, $R^1$, $R^2$, $R^3$ or $R^4$, together with the interconnecting atoms, may form a 3-, 4-, 5- or 6-membered ring, which

may be substituted ($R^5$ is preferably hydrogen or optionally substituted alkyl); and

$R^b$ is alkyl, alkenyl, alkynyl, carbocyclyl or heterocyclyl, each of which may be substituted; or hydrogen or acyl.

Preferred substituents on the 2-pyridyl group ($A^1$) are halogen, hydroxy, cyano, nitro, $SF_5$, trialkylsilyl, optionally substituted amino, acyl, or a group $-R^a$, $-OR^a$ or $-SR^a$, or a group $-C(R^a)=N-Q$, where Q is $-R^a$, $-OR^a$, $-SR^a$ or optionally substituted amino, wherein $R^a$ is alkyl, alkenyl, alkynyl, carbocyclyl or heterocyclyl, each of which may be substituted; or two adjacent substituents together with the atoms to which they are attached form an optionally substituted ring which can contain up to 3 hetero atoms. Especially preferred substituents are alkoxy, alkyl, cyano, halogen, nitro, alkoxycarbonyl, alkylsulfinyl, alkylsulfonyl and trifluoromethyl, particularly chlorine and trifluoromethyl.

Preferably, the 2-pyridyl group is substituted at the 3 and/or 5 position.

The invention also includes any of the compounds specifically exemplified hereinafter.

Any alkyl group may be straight or branched and is preferably of 1 to 10 carbon atoms, especially 1 to 7 and particularly 1 to 5 carbon atoms.

Any alkenyl or alkynyl group may be straight or branched and is preferably of 2 to 7 carbon atoms and may contain up to 3 double or triple bonds which may be conjugated, for example vinyl, allyl, butadienyl or propargyl.

Any carbocyclyl group may be saturated, unsaturated or aromatic, and contain 3 to 8 ring-atoms. Preferred saturated carbocyclyl groups are cyclopropyl, cyclopentyl or cyclohexyl. Preferred unsaturat d carbocyclyl groups contain up to 3 double bonds. A preferred aromatic carbocyclyl group is phenyl. The term carbocylic should be similarly construed. In addition, the term carbocyclyl includes any fused combination of carbocyclyl groups, for example naphthyl, phenanthryl, indanyl and ind nyl.

Any heterocyclyl group may be saturated, unsaturated or aromatic, and contain 5 to 7 ring-atoms up to 4 of which may be hetero-atoms such as nitrogen, oxygen and sulfur. Examples of heterocyclyl groups are furyl, thienyl, pyrrolyl, pyrrolinyl, pyrrolidinyl, imidazolyl, dioxolanyl, oxazolyl, thiazolyl, imidazolyl, imidazolinyl, imidazolidinyl, pyrazolyl, pyrazolinyl, pyrazolidinyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, thiadiazolyl, pyranyl, pyridyl, piperidinyl, dioxanyl, morpholino, dithianyl, thiomorpholino, pyridazinyl, pyrimidinyl, pyrazinyl, piperazinyl, sulfolanyl, tetrazolyl, triazinyl, azepinyl, oxazepinyl, thiazepinyl, diazepinyl and thiazolinyl. In addition, the term heterocyclyl includes fused heterocyclyl groups, for example benzimidazolyl, benzoxazolyl, imidazopyridinyl, benzoxazinyl, benzothiazinyl, oxazolopyridinyl, benzofuranyl, quinolinyl, quinazolinyl, quinoxalinyl, dihydroquinazolinyl, benzothiazolyl, phthalimido, benzofuranyl, benzodiazepinyl, indolyl and isoindolyl. The term heterocyclic should be similarly construed.

Any alkyl, alkenyl, alkynyl, carbocyclyl or heterocyclyl group, when substituted, may be substituted by one or more substituents, which may be the same or different, and may be selected from the list: hydroxy; mercapto; azido; nitro; halogen; cyano; acyl; optionally substituted amino; optionally substituted carbocyclyl; optionally substituted heterocyclyl; cyanato; thiocyanato; $-SF_5$; $-OR^a$; $-SR^a$ and $-Si(R^a)_3$, where $R^a$ is alkyl, alkenyl, alkynyl, carbocyclyl or heterocyclyl, each of which may be substituted. In the case of any carbocyclyl or heterocyclyl group the list includes additionally: alkyl, alkenyl and alkynyl, each of which may be substituted. Preferred substituents on any alkyl, alkenyl or alkynyl group are alkoxy, haloalkoxy or alkylthio, each containing 1 to 5 carbon atoms; halogen; or optionally substituted phenyl. Preferred substituents on any carbocyclyl or heterocyclyl group are alkyl, haloalkyl, alkoxy, haloalkoxy or alkylthio, each containing 1 to 5 carbon atoms; halogen; or optionally substituted phenyl.

In the case of any alkyl group or any unsaturated ring-carbon in any carbocyclyl or heterocyclyl group the list includes a divalent group such as oxo or imino, which may be substituted by optionally substituted amino, $R^a$ or $-OR^a$. Preferred groups are oxo, imino, alkylimino, oximino, alkyloximino or hydrazono.

Any amino group, when substituted and where appropriate, may be substituted by one or two substituents which may be the same or different, selected from the list: optionally substituted alkyl, optionally substituted amino, $-OR^a$ and acyl groups. Alternatively two substituents together with the nitrogen to which they are attached may form a heterocyclyl group, preferably a 5 to 7-membered heterocyclyl group, which may be substituted and may contain other hetero atoms, for example morpholino, thiomorpholino or piperidinyl.

The term acyl includes the residues of sulfur and phosphorus-containing acids as well as carboxylic acids. Typically the residues are covered by the general formulae $-C(=X^a)R^c$, $-S(O)_pR^c$ and $-P(=X^a)(OR^a)(OR^a)$, where appropriate $X^a$ is O or S, $R^c$ is as defined for $R^a$, $-OR^a$, $-SR^a$, optionally substituted amino or acyl; and p is 1 or 2. Preferred groups are $-C(=O)R^d$, $-C(=S)R^d$,and $-S(O)_pR^d$ where $R^d$ is alkyl, $C_1$ to $C_5$ alkoxy, $C_1$ to $C_5$ alkylthio, phenyl, heterocyclyl or amino, each of which may be substituted.

Complexes of compounds of the invention are usually formed from a salt of formula $MAn_2$, in which M is a divalent metal cation, e.g. copper, manganese, cobalt, nickel, iron or zinc and An is an anion, e.g. chloride, nitrate or sulfate.

In cases where the compounds of the invention exist as the E and Z isomers, the invention includes individual isomers as well as mixtures thereof.

In cases where compounds of the invention exist as tautomeric isomers, the invention includes individual tautomers as well as mixtures thereof.

In cases where the compounds of the invention exist as optical isomers, the invention includes individual isomers as well as mixtures thereof.

The compounds of the invention have activity as fungicides, especially against fungal diseases of plants, e.g. mildews and particularly cereal powdery mildew (*Erysiphe graminis*) and vine downy mildew (*Plasmopara viticola*), rice blast

(*Pyricularia oryzae*), cereal eyespot (*Pseudocercosporella herpotrichoides*), rice sheath blight (*Pellicularia sasakii*), grey mould (*Botrytis cinerea*), damping off (*Rhizoctonia solani*), wheat brown rust (*Puccinia recondita*), late tomato or potato blight (*Phytophthora infestans*), apple scab (*Venturia inaequalis*), and glume blotch (*Leptosphaeria nodorum*). Other fungi against which the compounds may be active include other powdery mildews, other rusts, and other general pathogens of Deuteromycete, Ascomycete, Phycomycete and Basidomycete origin.

The invention thus also provides a method of combating fungi at a locus infested or liable to be infested therewith, which comprises applying to the locus a compound of formula I.

The invention also provides an agricultural composition comprising a compound of formula I in admixture with an agriculturally acceptable diluent or carrier.

The composition of the invention may of course include more than one compound of the invention.

In addition, the composition can comprise one or more additional active ingredients, for example compounds known to possess plant-growth regulant, herbicidal, fungicidal, insecticidal, acaricidal, antimicrobial or antibacterial properties. Alternatively the compound of the invention can be used in sequence with the other active ingredient.

The diluent or carrier in the composition of the invention can be a solid or a liquid optionally in association with a surface-active agent, for example a dispersing agent, emulsifying agent or wetting agent. Suitable surface-active agents include anionic compounds such as a carboxylate, for example a metal carboxylate of a long chain fatty acid; an *N*-acylsarcosinate; mono- or di-esters of phosphoric acid with fatty alcohol ethoxylates or alkyl phenol ethoxylates or salts of such esters; fatty alcohol sulfates such as sodium dodecyl sulfate, sodium octadecyl sulfate or sodium cetyl sulfate; ethoxylated fatty alcohol sulfates; ethoxylated alkylphenol sulfates; lignin sulfonates; petroleum sulfonates; alkyl-aryl sulfonates such as alkyl-benzene sulfonates or lower alkylnaphthalene sulfonates, e.g.

butyl-naphthalene sulfonate; salts of sulfonated naphthalene-formaldehyde condensates; salts of sulfonated phenol-formaldehyde condensates; or more complex sulfonates such as the amide sulfonates, e.g. the sulfonated condensation product of oleic acid and *N*-methyl taurine; the dialkyl sulfosuccinates, e.g. the sodium sulfonate of dioctyl succinate; acid derivatives of alkyl glycosides and alkylpolyglycosides materials and their metal salts, e.g. alkyl polyglycoside citrate or tartrate materials; or mono-, di- and tri-alkyl esters of citric acid and their metal salts.

Nonionic agents include condensation products of fatty acid esters, fatty alcohols, fatty acid amides or fatty-alkyl- or alkenyl-substituted phenols with ethylene and/or propylene oxide; fatty esters of polyhydric alcohol ethers, e.g. sorbitan fatty acid esters; condensation products of such esters with ethylene oxide, e.g. polyoxyethylene sorbitan fatty acid esters; alkyl glycosides, alkyl polyglycoside materials; block copolymers of ethylene oxide and propylene oxide; acetylenic glycols such as 2,4,7,9-tetramethyl-5-decyne-4,7-diol, ethoxylated acetylenic glycols; acrylic based graft copolymers; alkoxylated siloxane surfactants; or imidazoline type surfactants, e.g. 1-hydroxyethyl-2-alkylimidazoline.

Examples of a cationic surface-active agent include, for instance, an aliphatic mono-, di-, or polyamine as an acetate, naphthenate or oleate; an oxygen-containing amine such as an amine oxide, polyoxyethylene alkylamine or polyoxypropylene alkylamine; an amide-linked amine prepared by the condensation of a carboxylic acid with a di- or polyamine; or a quaternary ammonium salt.

The compositions of the invention can take any form known in the art for the formulation of agrochemicals, for example, a solution, an aerosol, a dispersion, an aqueous emulsion, a microemulsion, a dispersible concentrate, a dusting powder, a seed dr ssing, a fumigant, a smoke, a dispersible powder, an emulsifiable concentrate, granules or an impr gnated strip. Moreover it can be in a suitable form for direct application or as a concentrate or primary composition which requires dilution with a suitable quantity of water or other diluent before

application.

A dispersible concentrate comprises a compound of the invention dissolved in one or more water miscible or semi-water miscible solvents together with one or more surface activeand/or polymeric material. Addition of the formulation to water results in the crystalisation of the active ingredient, the process being controlled by the surfactants and/or polymers resulting in a fine dispersion.

A dusting powder comprises a compound of the invention intimately mixed and ground with a solid pulverulent diluent, for example, kaolin.

An emulsifiable concentrate comprises a compound of the invention dissolved in a water-immiscible solvent which forms an emulsion or microemulsion on addition to water in the presence of an emulsifying agent.

A granular solid comprises a compound of the invention associated with similar diluents to those that may be employed in dusting powders, but the mixture is granulated by known methods. Alternatively it comprises the active ingredient absorbed or coated on a pre-formed granular carrier, for example, Fuller's earth, attapulgite, silica or limestone grit.

Wettable powders, granules or grains usually comprise the active ingredient in admixture with suitable surfactants and an inert powder diluent such as clay or diatomaceous earth.

Another suitable concentrate is a flowable suspension concentrate which is formed by grinding the compound with water or other liquid, surfactants and a suspending agent.

The concentration of the active ingredient in the composition of the present invention, as applied to plants is preferably within the range of 0.0001 to 1.0 per cent by weight, especially 0.0001 to 0.01 per cent by weight. In a primary composition, the amount of active ingredient can vary widely and can be, for example, from 5 to 95 per cent by weight of the composition.

The invention is generally applied to seeds, plants or their habitat. Thus, the compound can be applied directly to the soil before, at or after drilling so that the presence of active compound in the soil can control the growth of fungi which may attack seeds. When the soil is treated directly the active compound can be applied in any manner which allows it to be intimately mixed with the soil such as by spraying, by broadcasting a solid form of granules, or by applying the active ingredient at the same time as drilling by inserting it in the same drill as the seeds. A suitable application rate is within the range of from 5 to 1000 g per hectare, more preferably from 10 to 500 g per hectare.

Alternatively the active compound can be applied directly to the plant by, for example, spraying or dusting either at the time when the fungus has begun to appear on the plant or before the appearance of fungus as a protective measure. In both such cases the preferred mode of application is by foliar spraying. It is generally important to obtain good control of fungi in the early stages of plant growth, as this is the time when the plant can be most severely damaged. The spray or dust can conveniently contain a pre- or post-emergence herbicide if this is thought necessary. Sometimes, it is practicable to treat the roots, bulbs, tubers or other vegetative propagule of a plant before or during planting, for example, by dipping the roots in a suitable liquid or solid composition. When the active compound is applied directly to the plant a suitable rate of application is from 0.025 to 5 kg per hectare, preferably from 0.05 to 1 kg per hectare.

In addition, the compounds of the invention can be applied to harvested fruits, vegetables or seeds to prevent infection during storage.

In addition, the compounds of the invention can be applied to plants or parts thereof which have been genetically modified to exhibit a trait such as fungal and/or herbicidal resistance.

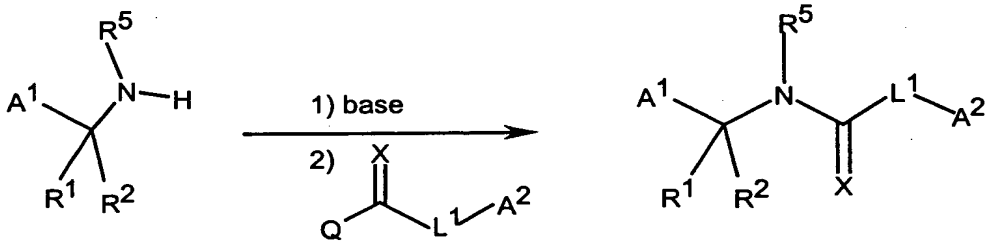
In addition th compounds of the invention can be used to treat fungal infestations in timber and in public health applications. Also the compounds of the invention can be used to treat insect and fungus infestations in domestic and farm animals.

Compounds of the invention may be prepared, in known manner, in a variety of ways.

Compounds of formula Ia, i.e. compounds of general formula I where L is $-N(R^5)C(=X)-L^1-$, where $L^1$ is $-CH(R^3)CH(R^4)-$, $-CH(R^3)-X^1-$ or $-C(R^3)=C(R^4)-$, may be prepared according to Scheme 1 by reacting compounds of formula II or their hydrochloride salt with compounds of formula III in the presence of a base, where Q is a leaving group such as halogen, preferably chlorine. A preferred base is triethylamine.

Compounds of formula III can prepared from the corresponding carboxylic acid by methods known to the skilled chemist. Compounds of formula III can either be isolated or generated *in situ*.

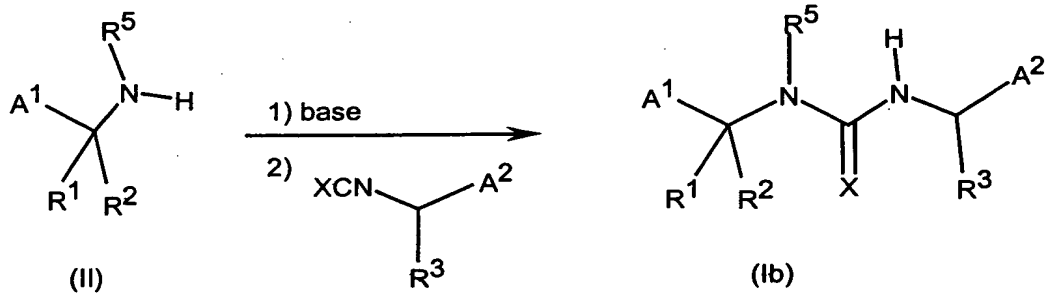
Scheme 1




(II) (III) (Ia)

Compounds of formula Ib, i.e. compounds of general formula I where L is $-N(R^5)C(=X)-NH-CH(R^3)-$, may be prepared according to Scheme 2 by reacting compounds of formula II or their hydrochloride salt with compounds of formula IV. A preferred base is triethylamine.

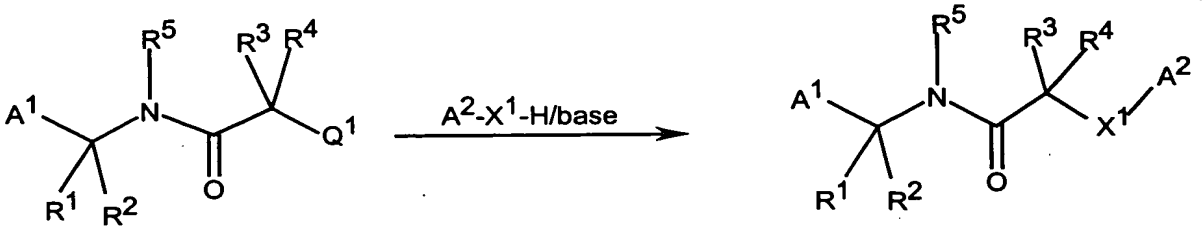
Scheme 2




(II) (IV) (Ib)

Compounds of formula Ic, i.e. compounds of g neral formula I where L is $-N(R^5)C(=X)-C(R^3)(R^4)-X^1-$ wherein $R^3$ and $R^4$ are not both hydrogen and X is oxygen, may also be prepared according to Scheme 3 by reacting compounds of formula V where $Q^1$ is a leaving group, preferably bromine, with $A^2-X^1-H$ in the presence of a suitable base, preferably potassium *tert*-butoxide.

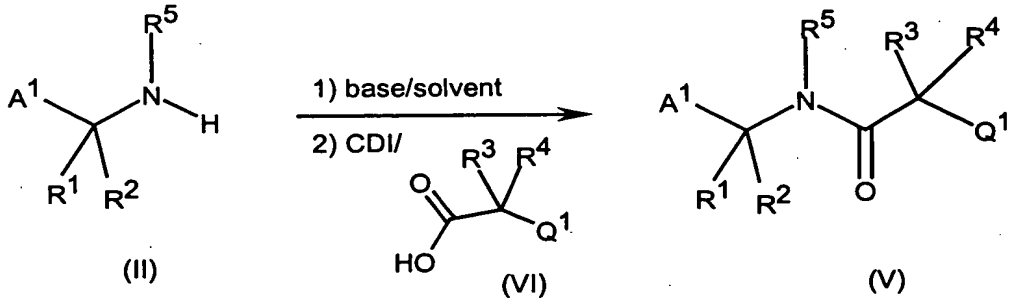
Scheme 3




(V) (Ic)

Compounds of formula V may be prepared according to Scheme 4 by reacting compounds of formula II in the presence of a suitable base such as triethylamine with compounds of formula VI, in the presence of a carbonyl diimidazole (CDI).

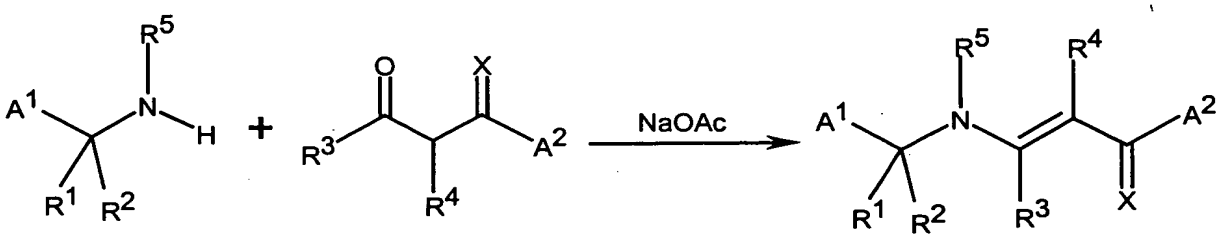
Scheme 4




(II) (VI) (V)

Compounds of formula Id, i.e. compounds of general formula I where L is $-N(R^5)C(R^3)=C(R^4)-C(=X)-$ wherein $R^3$ is not hydrogen, may be prepared according to Scheme 5 by reacting compounds of formula II or its hydrochloride salt in the presence of a suitable base such as sodium acetate with compounds of formula VII.

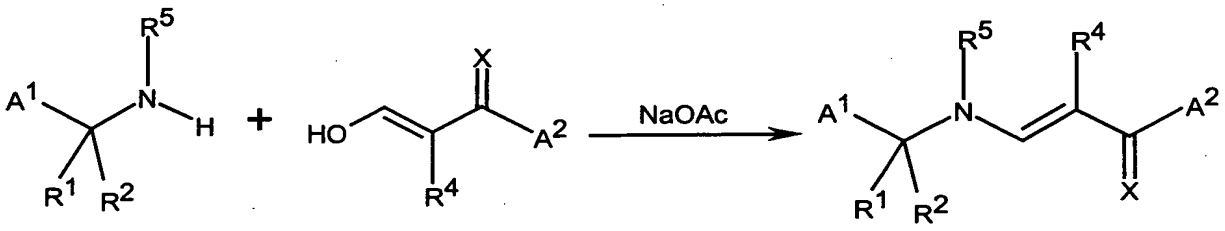
Scheme 5



(II) (VII) (Id)

Compounds of formula Ie, i.e. compounds of general formula I where L is $-N(R^5)CH=C(R^4)-C(=X)-$, may be prepared according to Scheme 6 by reacting compounds of formula II or its hydrochloride salt in the presence of a suitable base such as sodium acetate with compounds of formula VIII.

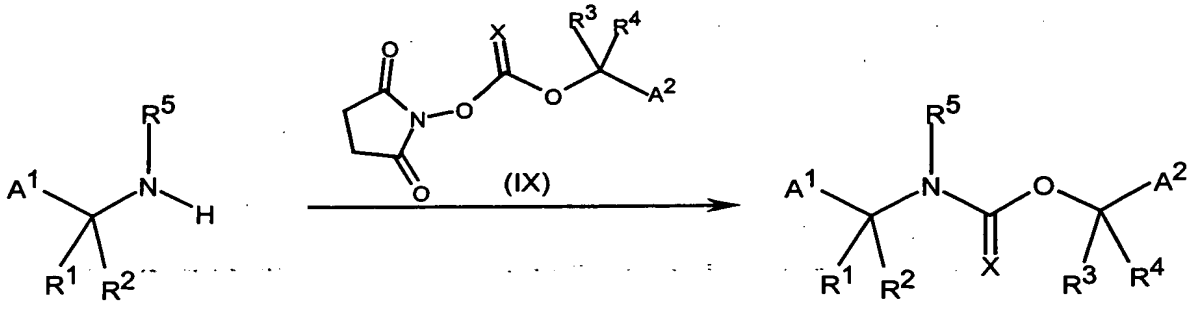
Scheme 6



(II) (VIII) (Ie)

Compounds of formula If, i.e. compounds of general formula I where L is $-N(R^5)C(=X)O-C(R^3)(R^4)-$, may be prepared according to Scheme 7 by reacting compounds of formula II or its hydrochloride salt in the presence of a suitable base such as triethylamine with compounds of formula IX.

Scheme 7



(II) (If)

Compounds of formula II may be prepared by methods described in international application PCT/GB/99/00304.

Other methods will be apparent to the chemist skilled in the art, as will be the methods for preparing starting materials and intermediates.

Collections of compounds of formula (I) may also be prepared in a parallel manner, either manually, automatically or semi-automatically. This parallel preparation may be applied to the reaction procedure, work-up or purification of products or intermediates. For a review of such procedures see by S.H. DeWitt in "Annual Reports in Combinatorial Chemistry and Molecular Diversity: Automated synthesis", Volume 1, Verlag Escom 1997, pages 69 to 77.

Furthermore, compounds of the formula (I) may be prepared using solid-supported methods, where the reactants are bound to a synthetic resin. See for example: Barry A. Bunin in "The Combinatorial Index", Academic Press, 1998 and "The tea-bag method" (Houghten, US 4,631,211; Houghten et al., Proc. Natl. Acad. Sci, 1985, 82, 5131-5135).

The preparation of the processes described herein yields compounds of the formula (I) in the form of substance collections which are termed libraries. The present invention also relates to libraries which comprise at least two compounds of the formula (I).

The invention is illustrated in the following Examples. Structures of isolated, novel compounds were confirmed by NMR and/or other appropriate analyses.

Example 1

*N*-[(3-Chloro-5-trifluoromethyl-2-pyridyl)methyl]-3-(2-tolyl)propionamide (Compound 2)

To a mixture of (3-chloro-5-trifluoromethyl-2-pyridyl)m thylamine hydrochloride (1 mmol, 0.247 g) in tetrahydrofuran (5 ml) was added triethylamine (2 mmol, 0.202 g) at room temperature and the mixture was stirred at room temperature for 1 hour. The mixture was filtered and the filtrat added to a solution of 3-(2-tolyl)propionyl chloride (1.1 mmol, 0.2 g) in tetrahydrofuran (5 ml) at room

temperature. After 4 hours stirring at room temperature th solvent was evaporated and the residue washed with water. The solid was filtered and washed with diethyl ether/light petroleum (1:20) to give the title product, m.p. 152-3 °C.

Example 2

*N*-Benzyl-*N'*-(3-chloro-5-trifluoromethyl-2-pyridyl)methylthiourea (Compound 4)

To a mixture of (3-chloro-5-trifluoromethyl-2-pyridyl)methylamine hydrochloride (0.12 g) and benzylisothiocyanate (0.11 g ) in dry tetrahydrofuran (10 ml) was added triethylamine (10 drops) and the mixture stirred at room temperature for 12 hours. The solvent was evaporated and ethyl acetate added. The mixture was washed with 2M hydrochloric acid and then with saturated sodium bicarbonate solution. The organic layer was separated and the solvent removed to give the title product, $^1$H N.M.R. δ(ppm) 4.7 (2H, broad s), 4.95 (2H, d), 6.9 (1H, broad s), 7.3-7.55 (6H, m), 7.95 (1H, s) and 8.58 (1H, s).

Example 3

*N*-[(3-Chloro-5-trifluoromethyl-2-pyridyl)methyl]-2-phenylthiopropanamide (Compound 15)

A mixture of thiophenol (55 mg) and potassium *tert*-butoxide (56 mg) in tetrahydrofuran (5 ml) was stirred at room temperature for 30 minutes. Starting material (see below) (173 mg) was added and the mixture was heated at 65 °C with stirring for 2 hours. When cool, the mixture was evaporated and the residue was purified by silica gel chromatography to give the title product, $^1$H N.M.R. δ(ppm) 1.6 (3h, d), 3.9 (1H, q), 4.67 (2H, d), 7.25 (3H, m), 7.38 (2H, m), 7.9 (1H, s), 8.0 (1H, broad s) and 8.7 (1H, s).

Preparation of starting material

*N*-[(3-Chloro-5-trifluoromethyl-2-pyridyl)methyl]-2-bromopropionamide

To a mixture of (3-chloro-5-trifluoromethyl-2-pyridyl)methylamine hydrochloride (1.0 g) in tetrahydrofuran (5 ml) and triethylamine (0.41 g) which had been stirred at room temperature for 30 minutes, was added a mixture of 2-bromopropionic acid (0.62 g) and carbonyldiimidazole (0.65 g)

in tetrahydrofuran (5 ml) which had also been stirred at room temperature for 30 minutes. The combined mixture was stirred at room temperatur for 12 hours and then the solvent was removed. The residue was partitioned between diethyl ether and water and the layers separated. The organic phase was dried ($MgSO_4$) and the solvent removed to give the title product.

Example 4

3-(3-Chloro-5-trifluoromethyl-2-pyridyl)methylamino)-1-phenylbut-2-enone (Compound 10)

To a suspension of (3-chloro-5-trifluoromethyl-2-pyridyl)methylamine hydrochloride (2.5 g) in dry tetrahydrofuran (20 ml) was added anhydrous sodium acetate (1.64 g) and benzoyl acetone (1.62g). The suspension was stirred at 20 °C for 18 hours, then heated at 50 °C for 4 hours. The mixture was evaporated and the residue partitioned between ethyl acetate and water. The organic extracts were dried ($MgSO_4$), filtered and evaporated to give a solid. The solid was triturated with diethyl ether, filtered and washed with diethyl ether to give the title product, m.p. 123-5 °C.

Example 5

3-(3-Chloro-5-trifluoromethyl-2-pyridyl)methylamino)-1-(2,6-dichlorophenyl)-propenone

(Compound 12)

The title compound was prepared in analogous fashion to Example 4 replacing benzoyl acetone with 1-(2,6-dichlorophenyl)-3-hydroxypropenone (see below). Purification was performed by silica gel chromatography eluting with 2% triethylamine in diethyl ether/light petroleum (b.p. 40-60 °C) (1:1) to give a mixture of E and Z isomers, $^1$H N.M.R. δ(ppm) 4.54 (2H, m, py-C$\underline{H}_2$), 4.76 (2H, m, py-C$\underline{H}_2$), 5.24 (1H, m, HNCH=C$\underline{H}$), 5.60 (1H, m, HNC$\underline{H}$=CH), 6.72 (1H, broad s, N$\underline{H}$), 7.02-7.35 (8H, m, 2xHNCH=C$\underline{H}$-, 6xAr-$\underline{H}$), 7.42 (1H, broad s, N$\underline{H}$), 7.96 (2H, d, 2xpy-$\underline{H}$), 8.7 (1H, s, py-$\underline{H}$), 8.86 (1H, s, py-H) and 10.5 (4H, broad s, 2x$N^+H_2Cl$).

Preparation of starting materials

a) 1-(2,6-Dichlorophenyl)-3-dimethylaminopropenone

To a solution of 2,6-dichloroacetophenone (2 g) in dry dimethylformamide dimethyl acetal (10 ml) was added pyridinium 4-toluene sulfonate (0.2 g). The mixture was stirred under nitrogen and heated to reflux for 90 minutes. An azeotrope of dimethylformamide dimethylacetal/methanol was distilled under nitrogen to complete loss of 2,6-dichloroacetophenone by thin layer chromatography. The cold mixture was evaporated to give a solid. The solid was triturated with 10% diethyl ether in light petroleum (b.p. 40-60 °C), filtered and washed with the same to give the title compound, m.p. 98-100 °C.

b) 1-(2,6-Dichlorophenyl)-3-hydroxypropenone

To a solution of the product from stage a) (1.2 g) in acetone (20 ml) and water (2 ml) was added dry Amberlyst 15 resin (2 g) and the mixture was refluxed with stirring under nitrogen for 18 hours. The solution was vacuum filtered and the filtrate evaporated. The residue was dissolved in diethyl ether (50 ml) and dried ($MgSO_4$). The filtrate was presorbed onto silica gel (10 g) and purified by silica gel chromatography gradient eluting with 20 to 30% diethyl ether in light petroleum (b.p. 40-60 °C) to give the title compound.

Example 6

(9-Fluorenylmethyl) *N*-[(3-Chloro-5-trifluoromethyl-2-pyridyl)methyl]carbamate (Compound 1)

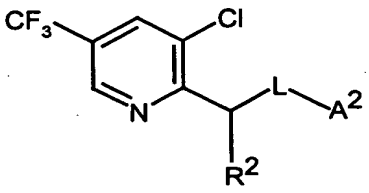
A mixture of the starting material (see below) (1.97 g), dioxane (40 ml), water (20 ml) and concentrated hydrochloric acid (10 ml) was refluxed for 48 hours. On cooling, diethyl ether (100 ml) was added and the layers separated. The organic layer was washed with water (50 ml), dried ($MgSO_4$) and the solvent removed to give a solid which was recrystallised from toluene, m.p. 159-61 °C.

Preparation of starting material

(9-Fluorenylmethyl) *N*-[(3-chloro-5-trifluoromethyl-2-pyridyl)-α-ethoxycarbonylmethyl]carbamate

To a mixture of 3-chloro-5-trifluoromethyl-2-pyridyl-α-ethoxycarbonylmethyl ammonium chloride (1.91 g) in dichloromethane (25 ml) and triethylamine (0.85 ml), was added *N*-(9-fluorenylmethoxycarbonyloxy)succinimide (2.02 g) and the mixture was stirred at room temperature for 90 minutes. Water (15 ml) was then added and the layers separated. The aqueous phase was extracted with dichloromethane and the combined organic layers were dried ($MgSO_4$) and the solvent removed. The residue was purified by silica gel chromatography gradient eluting with diethyl ether/light petroleum (b.p. 40-60 °C) to give the title compound.

The following compounds of formula Ig (see Table A), i.e. compounds of general formula I where $A^1$ is 3-Cl-5-$CF_3$-2-pyridyl and $R^1$ is hydrogen, may be prepared by methods analogous to the above Examples.

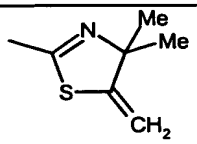



(Ig)

Table A

| Cmp | L | $R^2$ | $A^2$ | m.p. (°C) |
|---|---|---|---|---|
| 1 | -NH-C(=O)O-$CH_2$- | H | 9-fluorenyl | 159-61 |
| 2 | -NH-C(=O)-$(CH_2)_2$- | H | 2-tolyl | 152-3 |
| 3 | -NH-C(=O)NH-$CH_2$- | H | phenyl | oil |
| 4 | -NH-C(=S)NH-$CH_2$- | H | phenyl | oil |
| 5 | -NH-C(=O)NH-$CH_2$- | H | 3-Cl-5-$CF_3$-2-pyridyl | 153-4 |
| 6 | -N(Et)-C(=O)$CH_2$O- | $CO_2$Et | phenyl | 96-9 |
| 7 | -NH-C(=O)$CH_2$O- | H | phenyl | 123 |

| Cmp | L | $R^2$ | $A^2$ | m.p. (°C) |
|---|---|---|---|---|
| 8 | -NH-C(=O)$CH_2$S- | H | phenyl | 102-3 |
| 9 | -NHC(=O)CH=CH- | H | phenyl | 110-1 |
| 10 | -NHC(Me)=CH-C(=O)- | H | phenyl | 123-5 |
| 11 | -NHC(=O)CH=CH- | H | 2,6-diCl-phenyl | 168-9 |
| 12 | -NHCH=CH-C(=O)- | H | 2,6-diCl-phenyl | 129 |
| 13 | -NH-C(=O)-C(Me)$_2$O- | H | 4-Cl-phenyl | 65 |
| 14 | -NH-C(=O)-CH(Me)O- | H | 2,6-diCl-phenyl | 131 |
| 15 | -NH-C(=O)-CH(Me)S- | H | phenyl | oil |
| 16 | -NH-C(=O)$CH_2$O- | H | 2,4-diCl-phenyl | 149 |
| 17 | -NH-C(=O)$CH_2$O- | H | 4-Cl-phenyl | 116 |
| 18 | -NH-C(=O)$CH_2$S- | H | 3-(4-tolyl)-1,2,4-thiadiazol-5-yl | 162 |
| 19 | -NH-C(=O)$CH_2$O- | H | 4-tolyl | 116 |
| 20 | -NH-C(=O)$CH_2$O- | H | 4-Cl-benzthiazol-2-yl | 106 |
| 21 | -NH-C(=O)$CH_2$O- | H | 2-biphenylyl | 93 |
| 22 | -NH-C(=O)$CH_2$O- | H | 3,5-diCl-2-tolyl | 100 |
| 23 | -NH-C(=O)$CH_2$O- | H | 2-Cl-phenyl | 82 |
| 24 | -NH-C(=O)$CH_2$S- | H | 4,6-diCl-3-tolyl | 118 |
| 25 | -NH-C(=O)$CH_2$S- | H | 4-tolyl | 109 |
| 26 | -NH-C(=O)CH(Me)O- | H | 4-Cl-phenyl | oil |
| 27 | -NH-C(=O)CH(Me)O- | H | phenyl | 88 |
| 28 | -NH-C(=O)CH(Me)O- | H | 6-Cl-3-tolyl | oil |
| 29 | -NH-C(=O)CH(Ph)O- | H | 5-Cl-2-tolyl | 150 |
| 30 | -NH-C(=O)CH(-$CH_2$OMe)O- | H | 2,4,5-triCl-phenyl | 152 |
| 31 | -NH-C(=O)CH(Me)O- | H | 2-tolyl | 150 |
| 32 | -NH-C(=O)CH(-$CH_2$OMe)O- | H | 2,4-diCl-phenyl | 80 |
| 33 | -NH-C(=O)CH(Et)O- | H | 4-Cl-2-OH-phenyl | 83 |
| 34 | -NH-C(=O)CH(Ph)O- | H | 2,4,5-triCl-phenyl | 138 |
| 35 | -NH-C(=O)CH(Me)S- | H | 7-$CF_3$-quinolin-4-yl | 131 |
| 36 | -NH-C(=O)CH(Me)S- | H | benzthiazol-2-yl | 108 |
| 37 | -NH-C(=O)CH(Me)S- | H | 3-(2-Cl-phenyl)-1,2,4-thiadiazol-5-yl | oil |
| 38 | -NH-C(=O)CH(Me)S- | H | 2-M -1-Ph-1,2,4-triazol-3yl | oil |
| 39 | -NH-C(=O)CH(Me)S- | H | 3-Me-1,2,4-thiadiazol-5-yl | oil |

| Cmp | L | $R^2$ | $A^2$ | m.p. (°C) |
|---|---|---|---|---|
| 40 | -NH-C(=O)CH(Me)S- | H | 1-cyclohexyltetrazol-5-yl | oil |
| 41 | -NH-C(=O)CH(Me)S- | H |  | oil |
| 42 | -NH-C(=O)CH(Me)S- | H | 5-$CF_3$-benzthiazol-2-yl | 120 |
| 43 | -NH-C(=O)CH(Me)S- | H | 5-Cl-benzthiazol-2-yl | 132 |
| 44 | -NH-C(=O)CH(Me)S- | H | 2-pyridyl | oil |
| 45 | -NH-C(=O)CH(Me)S- | H | 1-Me-tetrazol-5-yl | 98 |
| 46 | -NH-C(=O)CH(Me)S- | H | 4,6-diMe-pyrimidin-2-yl | 132 |
| 47 | -NH-C(=O)CH(Me)S- | H | benzoxazol-2-yl | 72 |
| 48 | -NH-C(=O)CH(Me)S- | H | 2-MeO-phenyl | 100 |
| 49 | -NH-C(=O)CH(Me)S- | H | 1-Me-imidazol-2-yl | oil |
| 50 | -NH-C(=O)CH(Me)S- | H | 1-Me-1,3,4-triazol-2-yl | 98 |
| 51 | -NH-C(=O)CH(Me)S- | H | 5-$CF_3$-2-pyridyl | 98 |
| 52 | -NH-C(=O)CH(Me)S- | H | 5-Me-1,3,4-thiadiazol-2-yl | oil |
| 53 | -NH-C(=O)CH(Me)S- | H | 2-($CO_2$Me)-phenyl | 118 |
| 54 | -NH-C(=O)CH(Me)S- | H | 3-Cl-5-$CF_3$-2-pyridyl | 104 |
| 55 | -NH-C(=O)CH(Me)S- | H | 2-Cl-phenyl | 73 |
| 56 | -NH-C(=O)CH(Me)S- | H | 2,6-diCl-phenyl | 75 |
| 57 | -NH-C(=O)CH(Me)O- | H | 4-Br-3,5-diMe-phenyl | 121 |

Compound 3

$^1$H N.M.R. ($CDCl_3$) δ(ppm) 4.4 (2H, s), 4.7 (2H, s), 7.2-7.4 (5H, m), 7.9 (1H, s) and 8.65 (1H, s).

Compound 26

$^1$H N.M.R. ($CDCl_3$) δ(ppm) 1.55 (3H, d), 4.75 (3H, m), 6.8 (2H, d), 7.2 (2H, d), 7.7 (1H, br.s), 7.85 (1H, s) and 8.6 (1H, s).

Compound 28

$^1$H N.M.R. ($CDCl_3$) δ(ppm) 1.55 (3H, d), 2.3 (3H, s), 4.75 (3H, m), 6.65 (1H, m), 6.8 (1H, s), 7.2 (1H, m), 7.7 (1H, br.s), 7.85 (1H, s) and 8.6 (1H, s).

Compound 37

$^1H$ N.M.R. ($CDCl_3$) δ(ppm) 1.65 (3H, d), 4.6 (2H, d), 4.65 (1H, q), 7.25-7.45 (3H, m), 7.75 (1H, s), 7.8 (1H, s), 7.9 (1H, d) and 8.3 (1H, br.s).

Compound 38

$^1H$ N.M.R. ($CDCl_3$) δ(ppm) 1.55 (3H, d), 2.4 (3H, s), 4.3 (1H, q), 4.7 (2H, q), 7.3-7.5 (5H, m), 7.8 (1H, s), 8.15 (1H, s) and 8.4 (1H, br.s).

Compound 39

$^1H$ N.M.R. ($CDCl_3$) δ(ppm) 1.6 (3H, d), 2.6 (3H, s), 4.6 (1H, q), 4.65 (2H,s), 7.85 (1H, s), 8.1 (1H, br.s) and 8.65 (1H).

Compound 40

$^1H$ N.M.R. ($CDCl_3$) δ(ppm) 1.15-2.0 (13H, m), 4.0-4.1 (1H, m), 4.6 (2H, s), 7.8 (1H, s), 8.0 (1H, br.s) and 8.6 (1H, s).

Compound 41

$^1H$ N.M.R. ($CDCl_3$) δ(ppm) 1.25 (3H, s), 1.35 (3H, s), 1.5 (3H, d), 4.45 (1H, q), 4.75 (2H, qd), 5.05 (2H, d), 7.85 (1H, s), 8.15 (1H, br.s) and 8.6 (1H, s).

Compound 44

$^1H$ N.M.R. ($CDCl_3$) δ(ppm) 1.6 (3H, d), 4.5-4.75 (3H, m), 7.0 (1H, t), 7.1 (1H, m), 7.4 (1H, m), 7.8 (1H, s), 8.4 (1H, d), 8.55 (1H, s) and 8.7 (1H, br.s).

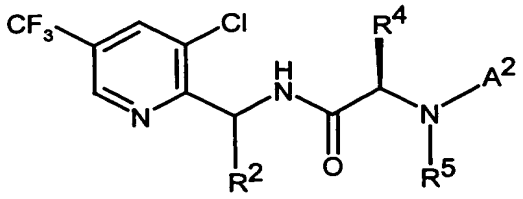
Compound 49

$^1H$ N.M.R. ($CDCl_3$) δ(ppm) 1.5 (3H, d), 3.5 (3H, s), 4.15 (1H, q), 4.6 (2H, qd), 6.8 (1H, s), 7.0 (1H, s), 7.8 (1H, s), 8.65 (1H, s) and 8.75 (1H, br.s).

Compound 52

$^1H$ N.M.R. ($CDCl_3$) δ(ppm) 1.6 (3H, d), 2.65 (3H, s), 4.65 (3H, m), 7.8 (1H, m), 8.15 (1H, br.s) and 8.6 (1H, s).

The following compounds of formula Ih (see Table B), i.e. compounds of general formula I where $A^1$ is 3-Cl-5-$CF_3$-2-pyridyl, $R^1$ is hydrogen and L is -NHC(=O)CH($R^4$)N($R^5$)-, may be prepared by methods analogous to the above Examples.

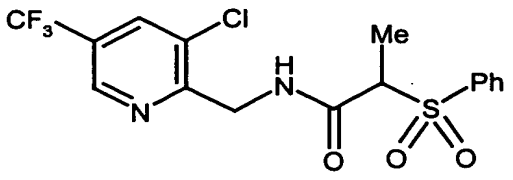


(Ih)

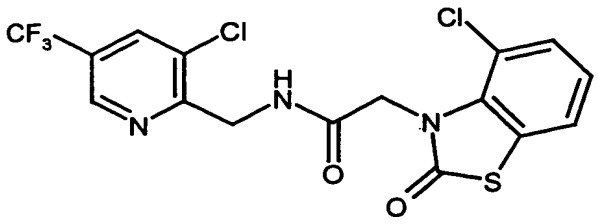
Table B

| Cmp | $R^2$ | $R^4$ | $R^5$ | $A^2$ | m.p. (°C) |
|---|---|---|---|---|---|
| 101 | H | H | H | 2-Me-benzoyl | 126 |
| 102 | H | Me (racemic) | H | benzyloxycarbonyl | 114 |
| 103 | H | $Pr^i$ | H | isopropyloxycarbonyl | 134 |
| 104 | H | $Bu^i$ | H | isopropyloxycarbonyl | 142 |
| 105 | H | $Bu^i$ | Me | isopropyloxycarbonyl | oil |
| 106 | Me | $Pr^i$ | H | isopropyloxycarbonyl | 151 |
| 107 | Me | $Bu^i$ | H | isopropyloxycarbonyl | 134 |
| 108 | Me | $Bu^i$ | Me | isopropyloxycarbonyl | oil |

Compound 201 m.p. 148 °C



Compound 202 m.p. 185 °C



Test Example

Compounds were assessed for activity against one or more of the following:

*Plasmopara viticola*: vine downy mildew
*Erysiphe graminis f. sp. tritici*: wheat powdery mildew
*Pyricularia oryzae*: rice blast
*Leptosphaeria nodorum*: glume blotch

Aqueous solutions or dispersions of the compounds at the desired concentration, including a wetting agent, were applied by spray or by drenching the stem base of the test plants, as appropriate. After a given time, plants or plant parts were inoculated with appropriate test pathogens before or after application of the compounds as appropriate, and kept under controlled environmental conditions suitable for maintaining plant growth and development of the disease. After an appropriate time, the degree of infection of the affected part of the plant was visually estimated. Compounds are assessed on a score of 1 to 3 where 1 is little or no control, 2 is moderate control and 3 is good to total control. At a concentration of 500 ppm (w/v) or less, the following compounds scored 2 or more against the fungi specified.

*Plasmopara viticola*:
6

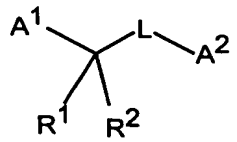
*Erysiphe graminis f. sp. tritici*:
3, 6 and 42

*Pyricularia oryzae*
6, 24, 45, 50 and 101

*Leptosphaeria nodorum*
26

Claims

1 The use of a compound of general formula I and salts thereof as a phytopathogenic fungicide



(I)

wherein

$A^1$ is 2-pyridyl or its *N*-oxide, each of which may be substituted by up to four groups at least one of which is haloalkyl;

$A^2$ is heterocyclyl or carbocyclyl, each of which may be substituted, or acyl;

L is a 4-atom linker selected from the list: $-N(R^5)C(=X)-X^1-CH(R^3)-$, $-N(R^5)C(=X)CH(R^3)CH(R^4)-$, $-N(R^5)C(=X)C(R^3)=C(R^4)-$, $-N(R^5)C(R^3)=C(R^4)-C(=X)-$, $-N(R^5)C(R^3)=C(R^4)-SO_2-$, $-N(R^5)C(=X)C(R^3)(R^4)-SO_2-$ and $-N(R^5)C(=X)C(R^3)(R^4)-X^1-$;

wherein $A^1$ is attached to the left hand side of linker L;

$R^1$, $R^2$, $R^3$ and $R^4$, which may be the same or different, are $R^b$, cyano, nitro, halogen, $-OR^b$, $-SR^b$ or optionally substituted amino; or $R^1$ and $R^2$, or $R^3$ and $R^4$, together with the interconnecting atoms, may form a 3-, 4-, 5- or 6-membered ring, which may be substituted;

X is oxygen or sulfur;

$X^1$ is oxygen, sulfur or $-N(R^5)-$;

$R^5$ is $R^b$, cyano or nitro, or $R^5$ and $A^2$, $R^1$, $R^2$, $R^3$ or $R^4$, together with the interconnecting atoms, may form a 3-, 4-, 5- or 6-membered ring, which may be substituted; and

$R^b$ is alkyl, alkenyl, alkynyl, carbocyclyl or heterocyclyl, each of which may be substituted; or hydrogen or acyl.

2 A pesticidal composition comprising at least one compound as claimed in claim 1 in admixture with an agriculturally acceptable diluent or carrier.

3 A method of combating pests at a locus infested or liable to be infested therewith, which comprises applying to the locus a compound as claimed in claim 1.